

**REMARKS**

Claims 1 through 18 are presently in the subject application.

Claims 10 through 15 have been amended to more fully define and more adequately protect Applicants' invention. The claims do not introduce new matter nor raise a new issue(s) and, accordingly, entry of these amendments is respectfully requested.

Applicants gratefully acknowledge the allowance of claims 1 through 9, 16 and 17.

Claims 10 through 15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rieveley, U.S. Patent No. 6,153,632 ("RIEVELEY") in view of Whitcomb, U.S. Patent No. 6,011,049 ("WHITCOMB") and Byrd, U.S. Patent No. 6,197,340 ("BYRD"). It is respectfully submitted that claims 10-15 are not obvious in view of these references when each is taken alone or in any combination.

The deficiencies of RIEVELEY, already of record are reiterated hereat. RIEVELEY reveals a composition for the treatment of diabetes mellitus which comprises (a) an insulin sensitizer and (b) a drug selected from insulin, injectable insulin, a sulfonylurea, a biguanide; and an alpha-glucosidase inhibitor. RIEVELEY does not reveal or hint at the combined, single integral unit of composition of medicaments as defined in claims 10 through 15. As previously indicated, RIEVELEY reveals a list of **ten (10)** insulin sensitizers one or more of which can be combined with one or more of (a) an injectable insulin, (b) a list of **six (6)** hypoglycaemics, (c) a list of two (2) biguanides, (d) a list of **three (3)** alpha-glucosidase inhibitors, and (e) a list of **twenty-six (26)** U.S. patents directed to orally administered insulins having at least **nine (9)** different classes of such compounds. One of ordinary skill in the art would have to pick and choose from a large number of combinations and permutations to arrive at the combination of medicaments of claims 10 through 15 from a view of RIEVELEY. *E.I. DuPont de Nemours &*

*Co. v. Ladd*, 140 U.S.P.Q. 297, 300-02 (C.A.D.C. 1964); *Bausch & Lomb V. Barnes-Hind/Hydrocurve*, 796 F.2d 443, 230 USPQ 416 (Fed. Cir. 1986). It is submitted that claims 10 through 15 are not obvious under 35 U.S.C. § 103(a) from a view of RIEVELEY.

Reference in this regard is also made to *Fujikawa v. Wattanasin*, 93 F.3d 1559, 39 USPQ 2d 1895, 1905 (Fed. Cir. 1996), where the CAFC stated,

...("Specific claims to single compounds require reasonably specific supporting disclosure and while ... *naming* [each species] is not essential, something more than the disclosure of a class of 1000, or 100, or even 48 compounds is required"). ...

Clearly, however, just because a moiety is listed as one possible choice for one position does not mean there is *ipsis verbis* support for every species or subgenus that chooses that moiety. Were this the case, a "laundry list" disclosure of every possible moiety for every possible position would constitute a written description of every species in the genus. This cannot be because such a disclosure would not "reasonably lead" those skilled in the art to any particular species. ...; and

to *In re Baird* 16 F.3d 380, 29 USPQ 2d 1550, 1552 (Fed. Cir. 1994), where the CAFC stated,

What a reference teaches is a question of fact. The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious. *In re Jones*, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992) (rejecting Commissioner's argument that "regardless [ ] how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it"). *Jones* involved an obviousness rejection of a claim to a specific compound... as obvious in view of, *inter alia*, a prior art reference

disclosing a genus which admittedly encompassed the claimed salt. We reversed the Board's rejection, reasoning that the prior art reference encompassed a "potentially infinite genus" of salts of dicamba and listed several such salts, but that it did not disclose or suggest the claimed salt. ...

In the instant case, the generic diphenol formula disclosed in Knapp contains a large number of variables, and we estimate that it encompasses more than 100 million different diphenols, only one of which is bisphenol A. While the Knapp formula unquestionably encompasses bisphenol A when specific variables are chosen, there is nothing in the disclosure of Knapp suggesting that one should select such variables. Indeed, Knapp appears to teach away from the selection of bisphenol A by focusing on more complex diphenols. ... Knapp teaches that in preferred diphenols, R has 2 to 4 carbon atoms and R' and R'' have 3 to 4 carbon atoms, and in "optimum" diphenols, R is an isopropylidene radical, R' and R'' are selected from the group consisting of propylene and butylene radicals, and n is one. ... Knapp further states that the diphenol in the preferred polyester material is ... Fifteen typical diphenols are recited. None of them, or any of the other preferred phenols recited above, is or suggests bisphenol A. ...

"[A] reference must be considered not only for what it expressly teaches, but also for what it fairly suggests." *In re Burckel*, 592 F.2d 1175, 1179, 201 USPQ 67, 70 (CCPA 1979). Given the vast number of diphenols encompassed by the generic diphenol formula in Knapp, and the fact that the diphenols that Knapp specifically discloses to be "typical," "preferred," and "optimum" are different from and more complex than bisphenol A, we conclude that Knapp does

not teach or fairly suggest the selection of bisphenol A. *See In re Belle* 991 F.2d 781, 26 USPQ2d 1529 (Fed. Cir. 1993) (DNA sequence would not have been obvious in view of prior art reference suggesting a nearly infinite number of possibilities and failing to suggest why among all those possibilities one would seek the claimed sequence). A disclosure of millions of compounds does not render obvious a claim to three compounds. ...

RIEVELEY reveals many combinations and thus does not render obvious the composition or a method of using such composition, as defined in claims 10 through 15.

The deficiencies of WHITCOMB already of record are reiterated hereat. WHITCOMB does not reveal or hint at the single integral unit composition as defined in claims 10 through 15.

One of ordinary skill in the art in viewing WHITCOMB would understand and appreciate that WHITCOMB is only revealing a conventional “combination therapy”, which involves administering two or more drugs **separately**. Combination therapy does not involve a **unitary** mixture of two or more drugs as defined by Applicants.

Nowhere in WHITCOMB is an actual combination of pioglitazone with metformin or with phenformin or buformin in a unitary composition described.

Why would a person of ordinary skill in the art combine RIEVELEY with WHITCOMB, when such person must pick and choose from the former a vast number of permutations and combinations to possibly find a proper composition formulation to apply with the “combination therapy” of the latter. It is respectfully submitted that such combination of references is possible only with the hindsight provided by Applicants’ disclosure.

Claims 10 through 15 are not rendered obvious, under 35 U.S.C. § 103(a), in view of RIEVELEY and WHITCOMB when each is taken alone or in combination.

BYRD does not reveal or hint at the unitary or single integral unit of the composition as defined by Applicants' in claims 10 through 15. BYRD reveals a controlled release formulation of lipoic acid (not claimed by Applicants). BYRD reveals that if the lipoic acid has insufficient blood glucose lowering effect then it is supplemented with sulfonylureas, biguanides and thiazolidiones . In this regard, reference is made to BYRD at col. 6, lines 60-63, where it is stated,

However, if an insufficient glucose lowering effect results the lipoic acid may be supplemental with one or more orally effective antidiabetic agents selected from the group **consisting** of sulfonylureas, biguanides and thiazolidiones....(emphasis added).

Claims 10-15 are defined in terms of "consisting essentially of" which does not present these claims to encompass lipoic acid since the addition thereof would materially affect the basic and novel characteristics of the composition defined in claims 10 through 15. As indicated in BYRD, a principal lipoic acid formulation or composition is described which lowers the blood glucose. It is only when such lowering is **insufficient** is a **supplement** added thereto. Applicants are claiming a principal (not supplement) composition in claims 10-15 to which neither lipoic acid nor any supplement is present.

The transitory term "consisting essentially of," as opposed to the term "comprising" or "consisting of" in a claim, is a term of art having an accepted meaning in chemical as well as pharmaceutical patent practice. *Carter-Wallace, Inc. v. Gillette Co.*, 531 F. Supp. 840, 874 n.29, 211 U.S.P.Q. 499, 527 n.29 (Mass. 1981).

A group of the Primary Examiners of the Patent Office, for their own guidance, adopted a code of terms to aid uniformity of practice, which explains that claim terms are to be interpreted as follows:

1. “comprising” and “comprising essentially” as leaving the claim open for the inclusion of unspecified ingredients even in major amounts;
2. “consisting of” as closing the claim to the inclusion of materials other than those recited except for impurities ordinarily associated therewith, and
3. recital of “essentially” along with “consisting of” as rendering the claim open only for the inclusion of unspecified ingredients which do not materially affect the basic and novel characteristics of the composition.

*Ex parte Davis & Tuukkanen*, 80 U.S.P.Q. 44, 450 (POBA 1948). The Court of Appeals for the Federal Circuit (“CAFC”) has adopted this interpretation, i.e., the term “consisting essentially of” excludes ingredients that materially affect the basic and novel characteristics of the claimed composition. *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 750 F.2d 1569, 224 U.S.P.Q. 409 (fed. Cir. 1984); *Water Technologies Corp. v. Calco Ltd.*, 850 F.2d 660, 7 U.S.P.Q. 2d 1097 (Fed. Cir. 1988) (the phrase “does not exclude the addition of an ingredient that does not materially affect the invention’s characteristics”).

It is respectfully submitted that claims 10-15 are not rendered obvious in view of BYRD.

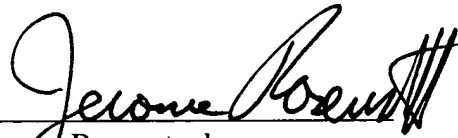
BYRD does not cure the deficiencies of RIEVELEY and WHITCOMB, as discussed above. BYRD does not provide a person of ordinary skill in the art a suggestion or rationale for combining any of these references in any manner. It is submitted that Applicants’ invention as defined in claims 10-15 is not rendered obvious, under 35 U.S.C. § 103(a), in view of

RIEVELEY, WHITCOMB and BYRD, when each of these references is taken alone or in any combination. Allowance of claims 10-15 is respectfully requested.

The Examiner is hereby authorized to call the undersigned attorney on record "collect" on any matter connected with this application. The telephone number is 212-588-0800. In the absence of the undersigned attorney of record, the call will be accepted by any attorney empowered in this application.

Respectfully submitted,

FROMMER LAWRENCE & HAUG, LLP  
Attorneys for Applicants

By   
Jerome Rosenstock  
Reg. No. 25,456  
(212) 588-0800